

IN THE CLAIMS:

Claim 1. (currently amended) A method for preventing or treating ototoxicity in a patient selected from the group consisting of a human, a cat, and a dog undergoing treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound, the method comprising administering to said patient an effective amount of an otoprotective agent comprising a compound containing a methionine or a methionine-like moiety having the structure formula:



|

Y

10

15

wherein m is an integer from 0 to 3; n is an integer from 1 to 3; X = -OR<sup>1</sup>, -

OCOR<sup>1</sup>, -COOR<sup>1</sup>, -CHO, -CH(OR<sup>1</sup>)<sub>2</sub>, or -CH<sub>2</sub>OH; Y = -NR<sup>2</sup>R<sup>3</sup> or -OH; R<sup>1</sup> = H or a

substituted or unsubstituted, straight or branched chain alkyl group having 1 to 6

carbon atoms; R<sup>2</sup> = H or a substituted or unsubstituted, straight or branched

chain acyl group having 1 to 6 carbon atoms; and R<sup>3</sup> = H or a substituted or

unsubstituted, straight or branched chain acyl group having 1 to 6 carbon atoms;

or

a pharmaceutically acceptable salt thereof.

Claim 2. (cancelled)

3. (currently amended) The method of claim 1 [[2]], wherein said otoprotective agent is selected from the group consisting of L-methionine, a mixture of D-methionine and L-methionine, normethionine, homomethionine, methioninol, hydroxy methionine, ethionine, S-adenosyl-L-methionine, a pharmaceutically acceptable salt thereof, and a combination thereof.

4. (currently amended) The method of claim 1 [[2]], wherein said otoprotective agent comprises L-methionine.

5. (currently amended) The method of claim 1 [[2]], wherein said otoprotective agent comprises a mixture of D-methionine and L-methionine.

6. (currently amended) The method of claim 1 [[2]], wherein said otoprotective agent comprises S-adenosyl-L-methionine.

7. (original) The method of claim 1, wherein said otoprotective agent is administered prior to the administration of said anti-tumor platinum-coordination compound.

8. (original) The method of claim 1, wherein said otoprotective agent is administered simultaneously with the administration of said anti-tumor platinum-coordination compound.

9. (original) The method of claim 1, wherein said otoprotective agent is administered subsequently to administration of said anti-tumor platinum-coordination compound.

10. (original) The method of claim 1, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 36 hours before administration of said anti-tumor platinum-coordination compound to about 36 hours after administration of said anti-tumor platinum-coordination compound.

11. (original) The method of claim 1, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 25 hours before administration of said anti-tumor platinum-coordination compound to about 25 hours after administration of said anti-tumor platinum-coordination compound.

12. (original) The method of claim 1, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 6 hours before administration of said anti-tumor platinum-coordination compound to about 6 hours after administration of said anti-tumor platinum-coordination compound.

13. (original) The method of claim 1, wherein said effective amount of said ototoxic agent is administered to said patient in a time period from about 1 hour before administration of said anti-tumor platinum-coordination compound to about 1 hour after administration of said anti-tumor platinum-coordination compound.

14. (original) The method of claim 1, wherein said effective amount of said ototoxic agent is administered to said patient in a time period from about one-half hour before administration of said anti-tumor platinum-coordination compound to about one-half hour after administration of said anti-tumor platinum-coordination compound.

15. (original) The method of claim 1, wherein said anti-tumor platinum-coordination compound is selected from the group consisting of *cis*-diamminedichloroplatinum(II), *trans*-diamminidichloroplatinum(II), *cis*-diammine-diaquaplatinum(II)-ion, chloro(diethyl-enetriamine)-platinum(II) chloride, dichloro(ethylene-diamine)-platinum(II), diammine(1,1-cyclobutanedi-carboxylato)-platinum(II), spiroplatin, dichlorotrans-dihydroxybis(isopropylamine platinum IV (iproplatin), diammine(2-ethylmalonato)-platinum(II), ethylenediamine-malonato platinum(II), aqua(1,2-diaminocyclohexane)-sulfatoplatinum(II), (1,2-diaminocyclohexane)malonato-platinum(II), (4-carboxy-phthalato)(1,2-diaminocyclohexane)-platinum(II), (1,2-diaminocyclohexane)-(isocitrate)platinum(II), (1,2-diaminocyclohexane)-*cis*(pyruvato)platinum(II), and (1,2-diaminocyclohexane)-oxalatoplatinum(II).

16. (original) The method of claim 15, wherein said anti-tumor platinum-coordination compound comprises *cis*-diamminedichloro-platinum(II).

17. (original) The method of claim 1, wherein said anti-tumor platinum-coordination compound is selected from the group consisting of cisplatin, carboplatin and iproplatin.

18. (original) The method of claim 1, wherein said otoprotective agent is administered parenterally, orally or topically to the round window membrane of said patient.

19. (original) The method of claim 18, wherein the administration of said effective amount of said otoprotective agent results in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 0.1 mg/kg body weight to about 500 mg/kg body weight.

20. (original) The method of claim 18, wherein the administration of said effective amount of said otoprotective agent results in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 1 mg/kg body weight to about 400 mg/kg body weight.

21. (original) The method of claim 18, wherein the administration of said effective amount of said otoprotective agent results in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 10 mg/kg body weight to about 300 mg/kg body weight.

22. (original) The method of claim 18, wherein the administration of said effective amount of said otoprotective agent results in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 10 mg/kg body weight to about 75 mg/kg body weight.

23. (original) The method of claim 1, wherein the molar ratio of the effective amount of said otoprotective agent to the effective amount of said anti-tumor platinum-coordination compound is from about 4:1 to about 167:1, otoprotective agent:platinum-coordination compound.

24. (original) The method of claim 1, wherein the molar ratio of the effective amount of said otoprotective agent to the effective amount of said anti-tumor platinum-

coordination compound is from about 4.25:1 to about 100:1, otoprotective agent:platinum-coordination compound.

25. (original) The method of claim 1, wherein the molar ratio of the effective amount of said otoprotective agent to the effective amount of said anti-tumor platinum-coordination compound is from about 4.68:1 to about 20:1, otoprotective agent:platinum-coordination compound.

26. (original) The method of claim 1, wherein the molar ratio of the effective amount of said otoprotective agent to the effective amount of said anti-tumor platinum-coordination compound is about 18.75:1, otoprotective agent:platinum-coordination compound.

27. (original) The method of claim 1, further comprising administering to said patient a supplemental amount of said otoprotective agent during and/or after the course of treatment with said anti-tumor platinum-coordination compound.

28. (original) The method of claim 27, wherein the supplemental amount of said otoprotective agent is administered orally, parenterally, or topically.

29. (original) The method of claim 28, wherein the administration of said supplemental amount of said otoprotective agent is sufficient to maintain an effective blood serum level of the otoprotective agent in said patient for a period of from one to fourteen days during and/or after the administration of said anti-tumor platinum-  
5 coordination compound.

30. (original) The method of claim 29, wherein the administration of said supplemental amount of said otoprotective agent results in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 0.1 mg/kg body weight to about 500 mg/kg body weight per week during and/or after the  
5 course of treatment with said anti-tumor platinum-coordination compound.

31. (original) A method for preventing or reducing ototoxicity in a patient selected from the group consisting of a human, a cat, and a dog undergoing treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound, the method comprising administering to said patient an effective amount of 5 an otoprotective agent comprising L-methionine, D,L-methionine or a pharmaceutically acceptable salt thereof, the administration of said effective amount of said otoprotective agent resulting in a blood serum level equivalent to that achieved by parenteral administration in the range of from about 1 mg/kg body weight to about 100 mg/kg body weight.

32. (currently amended) The method of claim 31, further comprising administering to said patient a supplemental amount of said otoprotective agent ~~after said noise exposure~~, the administration of said supplemental amount resulting in a blood serum level equivalent to that achieved by parenteral administration in the range 5 of from about 0.1 mg/kg body weight to about 500 mg/kg body weight per week after said noise exposure.

33. A method for preventing or treating ototoxicity in a patient undergoing treatment with an aminoglycoside antibiotic, the method comprising administering to said patient an effective amount of an otoprotective agent comprising methionine or a methionine-like moiety having the structural formula:

5 
$$\begin{array}{c} \text{CH}_3(\text{CH}_2)_m\text{S}(\text{CH}_2)_n\text{-CH-X} \\ | \\ \text{Y} \end{array}$$

wherein m is an integer from 0 to 3; n is an integer from 1 to 3; X = -OR<sup>1</sup>, -OCOR<sup>1</sup>, -COOR<sup>1</sup>, -CHO, -CH(OR<sup>1</sup>)<sub>2</sub>, or -CH<sub>2</sub>OH; Y = -NR<sup>2</sup>R<sup>3</sup> or -OH; R<sup>1</sup> = H or a 10 substituted or unsubstituted, straight or branched chain alkyl group having 1 to 6 carbon atoms; R<sup>2</sup> = H or a substituted or unsubstituted, straight or branched chain acyl group having 1 to 6 carbon atoms; and R<sup>3</sup> = H or a substituted or unsubstituted, straight or branched chain acyl group having 1 to 6 carbon atoms; or

15 a pharmaceutically acceptable salt thereof.

34. (cancelled)

35. (currently amended) The method of claim 33 [[34]], wherein said otoprotective agent is selected from the group consisting of L-methionine, normethionine, homomethionine, methioninol, hydroxy methionine, ethionine, S-adenosyl-L-methionine, a pharmaceutically acceptable salt thereof, and a combination 5 thereof.

36. (currently amended) The method of claim 33 [[34]], wherein said otoprotective agent comprises L-methionine.

37. (currently amended) The method of claim 33 [[34]], wherein said otoprotective agent comprises S-adenosyl-L-methionine.

38. (original) The method of claim 33, wherein said otoprotective agent is administered prior to the administration of said aminoglycoside antibiotic.

39. (original) The method of claim 33, wherein said otoprotective agent is administered simultaneously with the administration of said aminoglycoside antibiotic.

40. (original) The method of claim 33, wherein said otoprotective agent is administered subsequently to administration of said aminoglycoside antibiotic.

41. (original) The method of claim 33, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 36 hours before administration of said anti-tumor platinum-coordination compound to about 36 hours after administration of said aminoglycoside antibiotic.

42. (original) The method of claim 33, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 25 hours

before administration of said aminoglycoside antibiotic to about 25 hours after administration of said aminoglycoside antibiotic.

43. (original) The method of claim 33, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 6 hours before administration of said aminoglycoside antibiotic to about 6 hours after administration of said aminoglycoside antibiotic.

44. (original) The method of claim 33, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about 1 hour before administration of said aminoglycoside antibiotic to about 1 hour after administration of said aminoglycoside antibiotic.

45. (original) The method of claim 33, wherein said effective amount of said otoprotective agent is administered to said patient in a time period from about one-half hour before administration of said aminoglycoside antibiotic to about one-half hour after administration of said aminoglycoside antibiotic.